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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/478,099	01/05/2000	ANTHONY P. ADAMIS	50069/002002	1198

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Testa, Hurwitz, & Thibeault, LLP
125 High Street
High Street Tower
Boston, MA 02110

EXAMINER
FALK, ANNE MARIE

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/478,099	ADAMIS ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 January 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18 & 21* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *22* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendment filed November 20, 2002 (Paper No. 19) has been entered. Claims 1-18 have been amended. Claims 19 and 20 have been cancelled. Claim 21 has been newly added.

Claims 1-18 and 21 are pending in the instant application.

The following rejections are reiterated or newly applied and constitute the complete set of rejections being applied to the instant application. Rejections and objections not reiterated from the previous office action are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants are referred to the final guidelines on written description published January 5, 2001 in the Federal Register at Volume 66, Number 4, pp. 1099-1111 (also available at www.uspto.gov).

The newly added claim includes new matter.

Claim 21 recites elements without support in the original disclosure, thereby adding new matter to the claims. Claim 21 refers to a nucleic acid that reduces development of choroidal neovascularization. However, the specification fails to provide support for a nucleic acid that reduces development of choroidal neovascularization. As support for the newly added claim, Applicants point to the specification

at page 34, lines 10-14, but this section does not provide support for a nucleic acid that reduces development of choroidal neovascularization. Thus, Applicants have not pointed to adequate support for this amendment in the specification as-filed and the Examiner does not find specific support for this amendment.

Enablement

Claims 1-18 stand rejected and Claim 21 is rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 2-6 of the Office Action of Paper No. 10 (mailed 8/15/01) and on pages 3-8 of the Office Action of Paper No. 13 (mailed 5/21/02), and for the reasons set forth herein below, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

At pages 5-6 of the response, Applicants argue that the nucleic acid delivered to the eye need not be a gene that is expressed in cells, because an anti-vascular endothelial growth factor (VEGF) aptamer known as EYE001 can exert a therapeutic effect when administered by intravitreal injection. Applicants conclude that the specification fully enables one skilled in the art to practice the claimed method However, the instant specification does not disclose a VEGF aptamer nor discuss its use in the instantly claimed methods. Since the instant specification does not offer specific guidance to one skilled in the art with regard to specific nucleic acid molecules that could be used in the instantly claimed methods to produce a therapeutic effect or for diagnostic use, the specification fails to enable the full scope of the claimed invention. Furthermore, the specification does not enable the use of the claimed method for delivery of a VEGF aptamer because the specification does not contemplate delivery of a VEGF aptamer. Applicants arguments are not commensurate in scope with the scope of the claimed invention. The claimed invention covers the delivery of any nucleic acid molecule that may be used therapeutically or

diagnostically when delivered to the interior of the eye. However, the specification does not disclose a single nucleic acid that could be used in the claimed method for therapeutic or diagnostic purposes. Furthermore, it is well established that the specification must enable the full scope of the claimed invention. Although Applicants direct their arguments to nucleic acid molecules that need not be expressed *in situ*, the claims cover the use of nucleic acids that would require expression to be used for therapeutic or diagnostic purposes. It is further noted that the claims cover the use of nucleic acids larger than 150 kDa. Claims 5-18 and 21 do not recite an upper limit on the size of the nucleic acid to be delivered to the interior of the eye.

At page 7, paragraph 2 of the response, Applicants argue that the objection relating to the delivery of agents greater than 150 kDa is rendered moot by the amendment to Claim 1. However, Claims 5-18 and 21 do not recite an upper limit on the size of the nucleic acid to be delivered to the interior of the eye. Furthermore, Matsuo et al. (1996) disclose that plasmid DNA contacted to the outer surface of the eye does not get expressed in the interior of the eye. Specific types of liposomes must be used for the plasmid DNA to be delivered to the interior of the eye. Thus, the issue relating to the need for a means for facilitating transport of the nucleic acid across the sclera remains.

Written Description

Claims 1-18 stand rejected and Claim 21 is rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 8-10 of the Office Action of Paper No. 13 (mailed 5/21/02), as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants are referred to the final guidelines on written description published January 5, 2001 in the Federal Register at Volume 66, Number 4, pp. 1099-1111 (also available at www.uspto.gov).

At page 7, paragraph 5 of the response, Applicants assert that Claim 1 is directed to a method comprising contacting a scleral surface of the eye with a nucleic acid molecule having a molecular weight no greater than 150 kDa so that the nucleic acid can pass through the sclera into the interior of the eye. Applicants assert that the method may work for a variety of nucleic acids having the claimed features. No support is offered for this assertion. Furthermore, as noted above, Claims 5-18 and 21 do not recite an upper limit on the size of the nucleic acid to be delivered to the interior of the eye. Thus, Applicants arguments are not commensurate in scope with the scope of the claimed invention.

With regard to newly added Claim 21, the claim recites that the nucleic acid delivered "reduces development of choroidal neovascularization." However, the specification does not provide a written description of a nucleic acid molecule that "reduces development of choroidal neovascularization." Claims 16, 17, and 21 are directed to the treatment of specific diseases or broad classes of diseases, but the specification fails to provide a written description of nucleic acids that could be delivered to the interior of the eye, using the claimed method, to achieve a therapeutic result.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11, 14-18, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: a pump for facilitating transport of the nucleic acid through the sclera. The specification teaches that a pump is required to achieve delivery of the nucleic acid to the interior of the eye.

Claims 12 and 13 are indefinite in their recitation of "wherein the nucleic acid is delivered to the **sclera**" (emphasis added) because Claims 1 and 5 recite that "the nucleic acid passes **through** the sclera and into the interior of the eye" (emphasis added). Thus, the limitation recited in Claims 12 and 13 is in conflict with the limitations of Claims 1 and 5, which clearly recites delivery to the interior of the eye rather than to the sclera.

Claim 14 is indefinite in its recitation of "wherein the nucleic acid is delivered to by sclera" because the phrase is not grammatically correct and it is therefore unclear where the nucleic acid is delivered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 11, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Matsuo et al. (1996).

Matsuo et al. (1996) disclose the delivery of a nucleic acid to the retina of rats by liposome eye drops. The β-galactosidase gene was delivered to the retina by the installation of liposome eye drops containing the plasmid pCMV-beta. See Figures 1 and 2 on page 949. Thus, the method of Matsuo et al. includes contacting a scleral surface with a nucleic acid as recited in the instant claims.

Thus, the claimed invention is disclosed in the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Matsuo et al. (1996) and Faktorovich et al. (1990).

Claim 15 is directed to a method of delivering a nucleic acid molecule into a human eye by contacting a scleral surface of the eye with a nucleic acid molecule, so that the nucleic acid passes through the sclera and into the interior of the eye.

Matsuo et al. (1996) disclose the delivery of a nucleic acid to the retina of rats by liposome eye drops. The β-galactosidase gene was delivered to the retina by the installation of liposome eye drops containing the plasmid pCMV-beta. See Figures 1 and 2 on page 949. Thus, the method of Matsuo et al. includes contacting a scleral surface with a nucleic acid as recited in the instant claims.

Since the rat is considered an art-accepted animal model for studies of drug delivery to the eye and is particularly well suited as a model for certain human inherited retinal degenerations, as evidenced by Faktorovich et al. (1990), one of skill in the art would have been motivated to use the method of Matsuo et al. in humans and would have had a reasonable expectation of success for achieving similar gene transfer results in the human eye as found in the rat eye.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, William Phillips, whose telephone number is (703) 305-3482.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER